LISTING OF CLAIMS

The following listing of claims replaces all prior versions and listings of claims in the application.

1 - 18. (Canceled)

19. (Currently Amended) A method for measuring activity of PDH complex in a sample, said method comprising:

a) contacting a sample comprising PDH complex with an isolated antibody that specifically bind to PDH complex under conditions to allow formation of an immunocomplex of the antibody and the PDH complex present in the sample;

b) contacting the immunocomplex with a reaction mixture comprising a non-limiting amount of one or more substrates necessary for activity of the PDH complex; and

c) detecting:

(i) the amount of NADH produced in the reaction mixture, wherein the amount of NADH produced indicates the active state of the PDH complex, wherein detecting the amount of NADH produced comprises:

(1) directly measuring the amount of NADH formed; or

(2) indirectly measuring the amount of NADH formed by: transferring an electron from the newly formed reduced NADH to an electron acceptor molecule to produce NAD+, and determining a change indicating transfer of an electron to the electron acceptor molecule, wherein magnitude of the change indicates biological activity of the PDH complex; or

(ii) directly or indirectly the level of phosphorylation of immunocomplexed PDH complex ~~in the~~ in the sample as compared with that of an unphosphorylated PDH complex standard, wherein a level of phosphorylation greater than that in the standard indicates a lowered level of activity, and ~~a~~ the level of phosphorylation substantially equal to that of the PDH complex in the sample indicates a normal level of activity of the PDH complex in the sample~~;~~

~~wherein the detecting comprises:~~

~~(i) transferring an electron from reduced NADH to an electron acceptor molecule to produce NAD+; and~~

~~(ii) determining a change indicating transfer of an electron to the electron acceptor molecule, wherein magnitude of the change indicates biological activity of the PDH complex~~.

20. (Previously Presented) The method of claim 19, wherein the electron acceptor molecule is an electron acceptor dye molecule; and wherein determining a change indicating transfer of an electron involves monitoring the reaction mixture spectrophotometrically to detect a change in absorbance of the electron acceptor dye molecule; wherein magnitude of the change indicates biological activity of the PDH complex as compared to that of a comparable healthy sample of PDH complex.

21. (Previously Presented) The method of claim 20, wherein the electron acceptor dye molecule is resazurin.

22. (Original) The method of claim 20, wherein the monitoring comprises detecting a change in fluorescence from the dye molecule.

23. (Previously Presented) The method of claim 20, wherein the detecting comprises:

(i) contacting the reaction mixture with a PDH inhibitor and comparing an amount of resultant inhibition of the PDH complex compared to that of a comparable healthy sample of PDH complex, or

(ii) contacting the reaction mixture with a PDH complex activator and comparing an amount of resultant activation of the PDH complex compared to that of a comparable healthy sample of PDH complex.

24. (Previously Presented) The method of claim 23(i), wherein the PDH complex inhibitor is selected from sodium arsenite and ATP.

25. (Canceled)

26. (Previously Presented) The method of claim 23(ii), wherein the activator is dichloroactetate.

27 - 29. (Canceled)

30. (Previously Presented) The method of claim 19, further comprising:

separating remaining sample contents from the immunocomplex prior to detecting the level of phosphorylation of immunocomplexed PDH complex., wherein the level of phosphorylation is compared by measuring an amount of negative isoelectric point shift of the immunocomplexed PDH complex compared to the isoelectric point of the standard, the amount of negative isoelectric point shift being directly proportional to the amount of phosphorylation of the PDH complex in the sample.

31. (Original) The method of claim 30, wherein the sample is derived from a patient and wherein the amount of negative isoelectric shift is used to screen the patient for a disorder of PDH complex activity.

32. (Original) The method of claim 31, wherein the disorder is a disorder of energy production or utilization.

33. (Original) The method of claim 32, wherein the disorder is diabetes.

34. (Previously Presented) A method for screening to detect an active agent that modifies inhibitor or activator activity of a known inhibitor or activator of PDH complex comprising:

a) contacting a sample containing PDH complex in the presence of a known inhibitor or activator and a test active agent with a PDH complex immunoprecipitating antibody under conditions that allow formation of an antibody/PDH complex immunocomplex; and

b) determining the degree to which the test active agent modifies the inhibitor or activator activity of the known inhibitor or activator in the sample as compared to inhibitor or activator activity of the known inhibitor or activator in the absence of the test active agent, thereby detecting an active agent that modifies inhibitor or activator activity of a known inhibitor or activator of PDH complex.

35. (Canceled)

36. (Previously Presented) The method of claim 34, wherein:

(i) the PDH complex inhibitor is sodium arsenite or ATP and the test active agent decreases inhibitor activity of the PDH complex inhibitor; or

(ii) the PDH complex activator is dichloroactetate and the test active agent decreases activator activity of the PDH complex activator.

37. (Canceled)

38. (Previously Presented) The method of claim 34, wherein the antibody is an anti-E2 specific antibody, a monoclonal antibody, or a monoclonal anti-E2 specific antibody.

39 - 40. (Canceled)

41. (Original) A method for screening patients to identify patients suspected of having a late onset mitochondrial disorder, said method comprising:

a) contacting isolated antibodies that immunoprecipitate PDH complex with a patient sample comprising solubilized PDH complex so that the antibodies bind to solubilized PDH complex present in the sample to form an immunocomplex;

b) separating the immunocomplex from the remaining sample contents; and

c) detecting a decrease in the amount of PDH complex as compared with an amount in a corresponding normal sample, wherein the decrease indicates the patient is suspected of having the late onset mitochondrial disorder.

42. (Original) The method of claim 41, wherein the late onset mitochondrial disorder is selected from late onset diabetes, Huntington's, Parkinson's and Alzheimer's diseases, ALS (amyotrophic lateral sclerosis), and Schizophrenia.

43. (Previously Presented) The method of claim 41, wherein the separating comprises: separating the immunocomplex from other components of the sample using SDS-PAGE.

44. (Original) The method of claim 41, wherein the anti-PDH complex antibodies are attached to a solid support and the antibodies are tagged with a detectable marker.

45. (Previously Presented) The method of claim 44, wherein the detecting comprises:

contacting the immunocomplex with a detectable marker that binds specifically to the immunocomplex and measuring the amount of signal from the detectable marker present on the solid support.

46. (Previously Presented) The method of claim 44, wherein the solid support is beads or a microtiter plate.

47 - 48. (Canceled)

49. (Previously Presented) The method of claim 19, wherein the one or more substrates are β-NAD^+, Coenzyme A, FAD^+, cysteine, pyruvate, thiamine pyrophosphate (TPP), or two or more thereof.